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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/893,324 | 06/27/2001 | Laszlo Prokai | 1540/139 | 2061 |
| 2101 | 7590 | 11/12/2003 | EXAMINER | |
| BROMBERG & SUNSTEIN LLP 125 SUMMER STREET BOSTON, MA 02110-1618 | | | QAZI, SABIHA NAIM | |
| | | ART UNIT | | PAPER NUMBER |
| | | 1616 | | 13 |
| DATE MAILED: 11/12/2003 | | | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|-------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/893,324 | PROKAI ET AL. |
| | Examiner Sabiha Qazi | Art Unit 1616 |

-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 14 August 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1 and 5-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1, 5-9 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) The translation of the foreign language provisional application has been received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

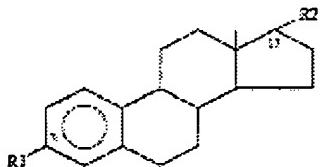
- | | |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ . |

Final Action on Merits

1. Acknowledgement is made of the response filed in paper no. 13, dated 8/14/03. Claims 1, and 5-9 are pending. Amendments are entered. Presently claimed invention of claim 1, 5-9 drawn to compounds and pharmaceutical formulations of estrogen (A ring is aromatic), having alkyl ether group at 17 position of the D ring such as 1, 3, 5(10) triene-3-ol-17-alkyl ether estradiols.
2. Rejection 35 U.S.C. 103(a) is maintained while other rejections are withdrawn because claims are amended. Rejection under 103 is maintained for the same reasons as set forth in our previous office action because arguments are not found persuasive.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. The disclosure is objected to because of the following informalities.
A typing error is noted on page 16, line 29. The 4e compound is hexyloxyestra derivative (see line12 on page 14) and not a butyloxyestra derivative.
Appropriate correction is required.
5. The reference Gridley et al. cited in line 18-19 on page 1 of the specification is incomplete as the Journal name is missing. Applicant is requested to provide a complete reference.
7. Claims 1 and 5-9 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Simpkins et al. (US 5,554,601). Simpkins et al. teach estra-17 substituted alkyl ether for neuroprotection and method for treating neurodegenerative diseases including Alzheimer's disease, which embraces Applicant's claimed invention. See the entire

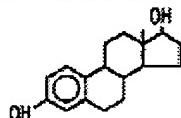
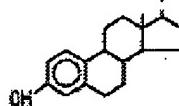
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document especially lines 11-54, col. 3; lines 1-42, col. 4; examples and claims
especially claim 4.



| R ₁ AND/OR R ₂ SUBSTITUTIONS | |
|--|--|
| NAME | STRUCTURE |
| HYDROXYL | -OH |
| METHYL | -CH ₃ |
| METHYL ESTER | -COCH ₃ |
| ACETATE | -C(=O)CH ₃ |
| ETHYL ETHER | -CH ₂ -CH ₃ |
| 3, 5, 6 (OR 6, 17) DIOLATE, METAL | $\text{HO}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{OH}$ |
| LINOLATE-D | $\text{HO}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}(\text{OH})-\text{C}(=\text{O})-\text{OH}$ |
| BENZYLIC | -C(=O)-CH ₂ -C ₆ H ₅ |
| BENZYL ETHER | -CH ₂ -C ₆ H ₅ |
| GLUCURONIDE | -C(=O)CH ₂ CO ₂ Na |
| SULFATE, SODIUM SALT | -C(=O)SO ₃ Na |
| OMEGA | -C(=O)CH ₂ CH ₂ CH ₂ ... |
| VALERATE | -C(=O)CH ₂ CH ₂ CH ₂ CO ₂ Na |
| CYCLOPENTYLPHOSPHATE | -C(=O)-CH ₂ -CH ₂ -C(=O)OPO ₃ Na |
| PROPRANOATE | -C(=O)-CH ₂ -CH ₂ -C(=O)CH ₂ CH ₃ |
| HEXANOATE | -C(=O)-CH ₂ -CH ₂ -C(=O)CH ₂ CH ₂ CH ₃ |
| VALERATE | -C(=O)-CH ₂ -CH ₂ -C(=O)CH ₂ CH ₂ CH ₂ CO ₂ Na |

| R ₁ AND/OR R ₂ SUBSTITUTIONS | |
|--|---|
| NAME | STRUCTURE |
| SODIUM PHOSPHATE | -O-PO ₃ Na ₂ |
| ENANTHATE | -C ₇ H ₁₂ O |
| GLUCURONIDE, SODIUM SALT | -C ₆ H ₁₀ O ₆ Na |
| STEARATE | -C ₁₈ H ₃₄ O |
| TRIETHYL AMMONIUM SALT | -N-(C ₂ H ₅) ₃ |
| CYPIONATE | |

17 β ESTRADIOL17 α ESTRADIOL

Instant claims are drawn to 17-substituted alkyl ether at D ring in a compound having aromatic ring A.

Instant claims differ from the reference by reciting specific species and/or a more limited subgenus than the reference. See formula in col. 4 and Figs 9A and 9B on sheets 9 and 10 where various substituents at R1 and/or R2 are listed, which includes valerate, stearate, and benzyl ether. Arguments that presently claimed invention disclaims methyl ether and ethyl ether at R 17 position, compounds are still considered

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obvious due to the reason cited above. Note, that US '601 teaches that "estrogen compound" is defined as any structure described in the 11th edition of "steroids" from Steraloids Inc. and is incorporated as a reference. See lines 50-67 in col. 4. In present application same reference is incorporated. Even though some compounds are disclaimed, other steroids are considered obvious.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

8. Claims 1, and 5-9 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Amended claims recite "a long chain saturated alkyl, a long chain unsaturated alkyl" is considered a new matter. There is no support for such a long chain alkyl group. Applicants must limit the claims according to the disclosure of the invention.

9. For everyone's convenience applicant should draw the structure of the estrogenic compounds in claim 1.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is 703-305-3910. The examiner can normally be reached on every business day..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


SABIHA QAZI, PH.D
PRIMARY EXAMINER